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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,953	01/29/2004	Amedeo Leonardi	20199/100M275-US1	4561
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DARBY & DARBY P.C. P.O. BOX 770 Church Street Station New York, NY 10008-0770			EXAMINER ROYDS, LESLIE A	
			ART UNIT 1614	PAPER NUMBER
			MAIL DATE 12/04/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/768,953

Applicant(s)

LEONARDI ET AL.

Examiner

Leslie A. Royds

Art Unit

1614

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 November 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): the rejection of claims 19-20 under 35 U.S.C. 103(a).
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: 19 and 20.
Claim(s) rejected: 1-8, 11-18, 28-30, 41 and 42.
Claim(s) withdrawn from consideration: 9-10, 21-27, 31-40, 43-58.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____

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Patent Examiner
Art Unit 1614

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Continuation of 11. does NOT place the application in condition for allowance because:

Applicant presents remarks directed to the rejection of claims 1-8, 11-20, 28-30, 41 and 42 under 35 U.S.C. 103(a), stating that the Bonney reference does not inherently disclose treatment of urinary incontinence in schizophrenic patients because Bonney et al. only establishes that 37% of schizophrenic patients experience urge incontinence, which is far below the 100% standard required for inherency. Applicant alleges that the disorder must necessarily be present when a patient is treated with a prior art compound and Bonney fails to establish that urinary incontinence must necessarily be present every time a patient is treated for schizophrenia. Applicant further submits that Bonney solely provides speculation as to the relationship between schizophrenia and urge incontinence and does not provide the "association" as asserted by the Examiner. Still further, Applicant submits that Bonney suggests the need for further experimentation into this relationship. Applicant asserts that Bonney, in fact, teaches away from the expectation that a psychiatric medication would be effective to treat urge incontinence because Bonney teaches that the psychiatric medications used in the studied patients did not have significant effects in relation to urinary incontinence. Applicant further relies upon the fact that clozapine, a known schizophrenic drug, induces urinary incontinence and, therefore, the artisan would not have expected that a compound effective to treat schizophrenia would be effective for treating urge incontinence. Lastly, Applicant states that, for these reasons supra, the combination of Cosford, Bonney and Nilvebrandt does not render the claims obvious.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

Initially, it is noted that, to establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* at 1269, 20 USPQ2d at 1749 (quoting *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981)).

In the instant case, Cosford provides the clear teaching that the instantly claimed compound (i.e., "MTEP") is, in fact, effective for treating all schizophrenic patients, i.e., 100% of schizophrenics, without exclusion. Of this entire schizophrenic population, Bonney provides the factual extrinsic evidence demonstrating that a subpopulation of schizophrenic patients also suffers concomitantly from urge incontinence. Accordingly, the suggestion of Cosford to use the claimed MTEP compound for treating any schizophrenic is a clear suggestion to use it in any subpopulation of schizophrenic patients, such as those patients also suffering from urge incontinence, with the reasonable expectation of the same (or at least substantially similar) level of efficacy in treating this subpopulation of patients as would be expected in the treatment of schizophrenic patients per se. Furthermore, since products of identical composition cannot have mutually exclusive properties when administered under identical conditions, or, as in the present case, the same host, whatever effect(s) the instantly claimed MTEP compound has in treating urinary incontinence must necessarily be present in the method disclosed by Cosford et al., absent factual evidence to the contrary.

Furthermore, though Applicant alleges that Bonney merely provides speculation as to the neurogenic nature of schizophrenic urinary incontinence caused by the same neurological abnormalities that result from schizophrenia itself, it is first noted that (1) Bonney explicitly discloses that a urodynamic study of the same has already documented the neurogenic nature of bladder dysfunction in these patients (p.244, col.1, para.2) and (2) Bonney also explicitly teaches in the Discussion at page 248 that, "In conclusion, schizophrenic patients had significantly more urge incontinence, bedwetting, and leakage of any type than the comparison patients with mood disorders. The high prevalence of urge incontinence supports our prediction that some of these schizophrenic patients will have detrusor hyperreflexia on urodynamic study." Accordingly, Bonney provides cogent technical reasoning supporting this prediction and/or postulate such that the article does provide a clear suggestion of the neurogenic nature of schizophrenic urinary incontinence. In other words, Bonney goes beyond mere speculation and clearly suggests this association between the two conditions.

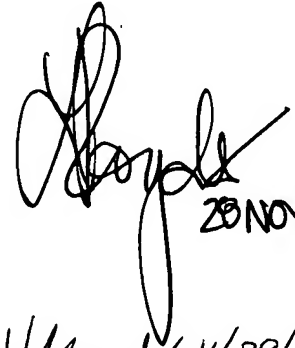
Moreover, Applicant alleges that Bonney, in fact, teaches away from the use of a psychiatric medication for the treatment of urge incontinence based upon the statement that, "All patients took psychiatric medication during the year prior to interview. There were no consistent significant effects of any class of medication in relation to urinary incontinence of the three types studied." However, this statement does not clearly establish that the instantly claimed compound did not have an effect in treating urinary incontinence. Absent this fact, and further absent any clear identification of which psychiatric medications were, in fact, used (note that Bonney generically teaches that subjects were asked to record usage of general classes of drugs, i.e., anti-psychotics, antiparkinson, antidepressants, lithium, antianxiety or other psychoactives), Applicant has failed to provide any basis to support the extrapolation of the lack of activity of "psychiatric medications" of any one or more of these general classes as being predictive of a lack of efficacy in using the claimed compound for treating schizophrenia and also having a beneficial effect upon urinary incontinence.

Lastly, Applicant again alleges that at least one antischizophrenic drug, clozapine, is known to induce urinary incontinence and, because of this fact, that the artisan would not have expected that a compound effective to treat schizophrenia would be effective for treating incontinence. However, as previously stated in the final rejection of June 14, 2007, Applicant provides no basis for extrapolating this evidence to the instantly claimed compound to support the conclusion that one of ordinary skill in the art at the time of the invention would have been led away from using MTEP in a schizophrenic patient because of an expectation of inducing urinary incontinence, not treating urinary incontinence. In addition, the fact remains that the clear efficacy of MTEP in treating schizophrenic patients would have been a clear suggestion to use it in any type of schizophrenic patient for this antipsychotic effect (including schizophrenic patients with concomitant urinary incontinence). Though the prior art establishes that one antipsychotic medication was known to induce urinary incontinence, this clearly falls short of establishing (1) that the art taught away from using MTEP for treating schizophrenic patients or (2) that MTEP itself induced urinary incontinence to such a degree that one of skill in the art would not have been motivated to use MTEP

for treating schizophrenics. Without this evidence, the claims remain obvious in view of the cited prior art.

Applicant's remarks with regard to the rejection of claims 19-20 over the combination of Cosford et al., Bonney et al. and Nilvebrandt et al. have been noted and are persuasive. Accordingly, the rejection of claims 19-20 is withdrawn. Claims 19-20 are now objected to for being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

For the reasons set forth supra, and those previously made of record in the final rejection of June 14, 2007, rejection of claims 1-8, 11-18, 28-30 and 41-42 remains proper and is maintained.



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11/28/07

ARDIAN H. MARSCHEL
SUPERVISORY PATENT EXAMINER